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| 10/614,362 | 07/07/2003 | Christopher J. M. Meade | 1/1363 | 7889 |

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| EXAMINER | |
|---|---|
| SPIVACK, PHYLLIS G | |
| **ART UNIT** | **PAPER NUMBER** |
| 1614 | |

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/614,362 | MEADE ET AL. | |
| | Examiner | Art Unit | |
| | Phyllis G. Spivack | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12-2-04;*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *9-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-3-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A Reply to the Restriction Requirement filed April 22, 2005 is acknowledged. Applicants have elected with traverse Group I, claims 1-8 and 35-37 drawn to pharmaceutical compositions, kits and therapeutic methods thereof.

Applicants argue Groups I and II are sufficiently related such that the search for relevant art for one Group would be expected to uncover prior art that is relevant to the other Group. Applicants urge a search for both Groups would not be an undue burden on the Examiner. As evidenced by the claims in U.S. Patents 6,492,377 and 6,265,612, subject matter directed solely to inhalants is recognized in the art as being divergent with a search requirement that is not co-extensive with other pharmaceutical compositions. There are separate and distinct considerations that do not apply to compositions intended for other modes of administration.

Applicants' argument is not found persuasive. The search burden is considered to be unduly extensive with respect to subject matter presented in claims 1-37.

Accordingly, the Restriction Requirement is proper and is hereby made FINAL. Claims 9-34 are withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as drawn to non-elected subject matter. All objections and rejections set forth in the first Office Action directed to claims that are presently withdrawn are withdrawn. Claims 1-8 and 35-37, drawn to pharmaceutical compositions, other than inhalants, kits, other than inhalants, and therapeutic methods thereof, represent the subject matter presently under consideration.

Re-affirmation of the election is requested when Applicants respond to this Office Action.

An Information Disclosure Statement filed November 3, 2004 is further acknowledged and has been reviewed.

It is noted the Request to add an omitted inventor filed March 8, 2004 is incomplete. See 37 CFR 1.48.

The requested structures of the following compounds: BIIF 1149, CP-122721, FK-888, NKP 608C, NKP 608A, CGP 60829, SR 48968, SR 140333, LY 303 870, MEN-11420, SB 223412, MDL-105172A, MDL-103896, MEN-11149, MEN-11467, DNK 333A, SR-144190, YM-49244, YM-44778, ZM-274773, MEN-10930, S-19752, YM-35275, DA-5018, MK-869, L-754030, CJ-11974, L-758298, DNK-33A, 6b-I, CJ-11974, TAK-637, GR 205171, are noted.

Claims 1-37 were rejected under 35 U.S.C. 112, second paragraph, in the last Office Action as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention with respect to the recitations "preferably" and "general formula".

Following the deletion of the recitations, this rejection of record is withdrawn.

Claims 4 and 5 were rejected under 35 U.S.C. 112, both first and second paragraphs, in the last Office Action, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the invention, and for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention with respect to the definition of "arylglycinamide derivatives of general formula 3".

Following the deletion of the term "derivatives", these rejections of record are withdrawn.

In the last Office Action claim 35 was rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is directed to the treatment and/or prevention of any inflammatory or obstructive disease of the respiratory tract. The specification provides support for a capsule formulation of N-[2-(3,5-bis-trifluoromethylphenyl)ethyl]-2-{4-[3-hydroxypropyl)-methylamino]piperidin-1-yl}-N-methyl-2-phenylacetamide. No support is provided for the combination of the compound referenced *supra* and any compound of instant formula 1 for the prevention of any inflammatory or obstructive disease of the respiratory tract.

It was asserted the instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation.

Applicants argue treating or preventing need not involve a cure of the diseases encompassed in the language of the claim, but merely show a reasonable likelihood of alleviating some condition associated with inflammatory or respiratory diseases.

Applicants' argument is not persuasive. The rejection is maintained for the reasons of record. Each particular disease or disorder of the respiratory tract has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed. The broad

recitation "treating or preventing any inflammatory or obstructive disease of the respiratory tract" is inclusive of many conditions that presently have no established successful therapies. The art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy. Further, there are no working examples to support a treatment modality comprising administering the claimed drug combination.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicants are advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Meissner et al., U.S. Patent 6,706,726, has a common assignee and inventor with the instant application. Based upon the earlier U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a)

might be overcome by (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of the invention for the claimed subject matter of the application that corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a Terminal Disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP 706.02(l)(1) and 706.02(l)(2), i.e., "In order to be disqualified as prior art under 35 U.S.C. 103(c), the subject matter that would otherwise be prior art to the claimed invention and the claimed invention must be commonly owned at the time the claimed invention was made or subject to an obligation of assignment that would establish common ownership.

Claims 1-8 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over both Meissner et al., U.S. Patent 6,706,726, and Pairet et al., U.S. Patent 6,620,438.

Meissner teaches the administration of the anticholinergics of formula 1 for use in the treatment of asthma and COPD. See, Example 1, column 10, column 19, lines 58-65, column 22, line 25, to column 25, line 20.

Meissner further teaches that the composition may be administered by inhalation and may be presented in the form of a solution, suspension or powder suitable therefor.

See column 22, lines 24-29, column 23, line 30 and column 24, line 43 to column 25, line 22.
See, in particular, column 20, lines 13-14, where "other pharmacologically active substances" may be combined.

The claims differ in that Meissner fails to teach combination with one or more $NK_1$ receptor antagonists. However, Pairet teaches the administration of pharmaceutical compositions comprising anticholinergics and the same $NK_1$ receptor antagonists that are presently claimed. See column 1, line 65, to column 2, line 20. Therefore, one skilled in the art would have been motivated to combine an anticholinergic of formula 1 with an $NK_1$ receptor antagonist in view of the combined teachings of Meissner and Pairet. Such would have been obvious in the absence of evidence to the contrary, because both references are drawn to treatment of respiratory tract diseases. Pairet teaches a synergistic effect of the combination of an anticholinergic and specific $NK_1$ receptor antagonists and thus provides motivation to combine such active agents. Meissner teaches the presently claimed anticholinergics specifically for use in the treatment of inflammatory or obstructive diseases of the respiratory tract. The determination of both optimal weight ratios and dosages are parameters well within the purview of those skilled in the art through no more than routine experimentation. Formulations prepared as kits are conventional packaging.

Claims 1-8 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banholzer et al., U.S. Patent 5,770,739, and Pairet et al., U.S. Patent 6,620,438. Banholzer teaches the administration of the presently claimed compounds of formula 1 to treat bronchitis and asthma. See column 1, line 11, to column 2, line 45. X is an

anion such as bromide. The compounds may be administered in pharmaceutically acceptable compositions, including preparations for inhalation. The claims differ in that Banholzer fails to teach combination with one or more $NK_1$ receptor antagonists. However, Pairet teaches the administration of pharmaceutical compositions comprising anticholinergics and the same $NK_1$ receptor antagonists that are presently claimed. See column 1, line 65, to column 2, line 20. Therefore, one skilled in the art would have been motivated to combine an anticholinergic of formula 1 with an $NK_1$ receptor antagonist in view of the combined teachings of Meissner and Pairet. Such would have been obvious in the absence of evidence to the contrary, because both references are drawn to treatment of respiratory tract diseases. Pairet teaches a synergistic effect of the combination of an anticholinergic and specific $NK_1$ receptor antagonists and thus provides motivation to combine such active agents. Meissner teaches the presently claimed anticholinergics specifically for use in the treatment of inflammatory or obstructive diseases of the respiratory tract. The determination of both optimal weight ratios and dosages are parameters well within the purview of those skilled in the art through no more than routine experimentation. Formulations prepared as kits are conventional packaging.

Claims 1-37 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of Pairet et al., U.S. Patent No. 6,455,524, in view of Banholzer et al., S.N. 10/391735, in the last Office Action. It was asserted Pairet teaches the administration of pharmaceutical compositions comprising anticholinergics and $NK_1$ receptor

antagonists for use in the treatment of respiratory tract diseases. Both the dosage forms and $NK_1$ receptor antagonists are those presently claimed.

The rejection is withdrawn because in Pairet et al., U.S. Patent No. 6,455,524, the anticholinergic agent, tiotropium, is not encompassed in instant formula 1.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 37 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 11/117,163, in view of Pairet et al., U.S. Patent 6,620,438. Although the conflicting claims are not identical, they are not patentably distinct from each other. The compound of formula 1 of the co-pending claims encompasses compounds of formula 1 of the present claims. See Example 1, page 15, of the co-pending specification where the structure "scopine-2,2-diphenylpropionate methobromide" is shown. X is bromide; A is an epoxide; $R^1$ and $R^2$ are methyl; $R^{3-6}$ are hydrogen; $R^7$ is methyl. The employed open language allows for the inclusion of any

number of additional active agents. It would have been obvious to administer the $NK_1$ receptor antagonists as disclosed by Pairet because they were known for use in the treatment of respiratory obstructive and inflammatory diseases as COPD.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-8 and 35-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9, 11 and 21-24 of Meissner et al., U.S. Patent No. 6,706,726, in view of Pairet et al., U.S. Patent 6,620,438. Although the conflicting claims are not identical, they are not patentably distinct from each other because compounds of formula 1 of the present claims are encompassed by formula 1 of Meissner. See Example 1, column 10, where the structure "scopine –2,2-diphenylpropionate methobromide" is shown. X is bromide; A is an epoxide; $R^1$ and $R^2$ are methyl; $R^{3-6}$ are hydrogen and $R^7$ is methyl. The employed open language allows for the inclusion of any number of additional active agents. It would have been obvious to administer the $NK_1$ receptor antagonists as disclosed by Pairet because they were known for use in the treatment of respiratory obstructive and inflammatory diseases as COPD.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached Monday to Friday from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

July 21, 2005